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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,930	12/26/2001	Masayo Kondo	029650-111	8178

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,930	KONDO ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 12-3-03 is acknowledged.

Claims included in the prosecution are 1 and 4-18. Applicant indicates that claim 1 as 'original'. It should have been 'currently amended' since the percentages are now introduced.

Claim Rejections - 35 USC ' 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 4-5, 7, 10-11, 13-16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 636 363.

EP discloses a liposomal composition, which selectively accumulates at the injured portion of vascular endothelium. The compositions contain a basic compound, a membrane forming phospholipid and a constituent of the membrane, cholesterol. Among the phospholipids taught are phosphatidylcholine, phosphatidylglycerol and acidic phosphatidic acid. The composition can further include surface modifying agents such as neuraminic acid (carboxyl group containing). The basic compounds include primary, secondary and tertiary amines and quaternary

amines. According to EP the drug can be any drug and includes glycosaminoglycan, heparin; the diagnostic agents include X-ray contrast agents (Note the abstract, page 4, lines 19-57, page 5, lines 21-42; and Examples, Example 3 in particular).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant admits that EP teaches the claimed components, but argues that the reference fails to teach the claimed percentages. The reference teaches the amounts in molar quantities and not in mole percentages (examples) and it would appear that they fall within the broad ranges and therefore, the rejection is maintained. The rejection however, will be reconsidered, if applicant shows that the molar quantities do not correspond to instant mole percentages.

3. Claims 1, 4-5, 7, 10-16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 09 263579.

JP discloses liposomal composition containing the basic compound, piperidine derivative (claimed compound of the formula 2) to deliver a therapeutic agent to the diseased part. The drugs include polynucleotides, genes, antioxidants, glycosaminoglycans or diagnostic agents. The liposomes contain a phospholipid, and a constituent of the membrane, cholesterol. Among the phospholipids taught are phosphatidylcholine, phosphatidylglycerol and acidic phosphatidic acid. The composition can further include surface modifying agents such as neuraminic acid (carboxyl group containing compound) (note the abstract and the entire English translation).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant admits that JP teaches the claimed components, but argues that the reference fails to teach the claimed percentages. The reference teaches the amounts in terms of 'grams' and not in mole percentages (examples) and it would appear that they fall within the broad ranges and therefore, the rejection is maintained. The rejection however, will be reconsidered, if applicant shows that the weight in grams in the reference does not correspond to instant mole percentages.

Claim Rejections - 35 USC ' 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 4-5, 7 and 10-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 636 363.

As pointed out above, EP discloses a liposomal composition, which selectively accumulates at the injured portion of vascular endothelium. The compositions contain a basic compound, a membrane forming phospholipid and a constituent of the membrane, cholesterol. Among the phospholipids taught are phosphatidylcholine, phosphatidylglycerol and acidic phosphatidic acid. The composition can further include

surface modifying agents such as neuraminic acid (carboxyl group containing). The basic compounds include primary, secondary and tertiary amines and quaternary amines. According to EP the drug can be any drug (Note the abstract, page 4, lines 19-57, page 5, lines 21-42; and Examples). Although EP does not exemplify the invention using an acidic phospholipid or using the surface modifier, neuraminic acid, it would have been obvious to one of ordinary skill in the art to prepare liposomal compositions containing these compounds from the guidance provided by EP with the expectation of obtaining similar results. EP does not teach specifically teach chondroitin sulfate as the glycosaminoglycan. However, in view of EP=s teachings of the use any glycosaminoglycans, one of ordinary skill in the art would have been motivated to use any glycosaminoglycan with a reasonable expectation of success.

6. Claims 1-5, 7 and 10-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 09-263579 cited above.

As pointed out above, JP discloses liposomal composition containing the basic compound, piperidine derivative (claimed compound of the formula 2) to deliver a therapeutic agent to the diseased part. The liposomes contain a phospholipid, and a constituent of the membrane, cholesterol. Among the phospholipids taught are phosphatidylcholine, phosphatidylglycerol and acidic phosphatidic acid. The composition can further include surface modifying agents such as neuraminic acid (carboxyl group containing compound). Although JP does not exemplify the invention using the acidic phospholipid, phosphatidic acid or using the surface modifier, neuraminic acid, it would have been obvious to one of ordinary skill in the art to prepare

liposomal compositions containing these compounds from the guidance provided by EP with the expectation of obtaining similar results. JP does not teach specifically teach chondroitin sulfate as the glycosaminoglycan. However, in view of JP=s teachings of the use any glycosaminoglycans, one of ordinary skill in the art would have been motivated to use any glycosaminoglycan with a reasonable expectation of success.

Applicant's arguments to the above 103 rejections have been fully considered, but are not found to be persuasive. Applicant argues that there is no suggestion in EP or JP to combine such compounds in specified amounts to make the liposome surface electrically neutral in the physiological pH condition and electrically cationic in acidic condition, and the capability of exhibiting the target directivity promptly by the pH change. These arguments are not persuasive. First of all, both EP and JP teach the targeted delivery of the drugs and both teach the presence of the claimed components and varying the amounts to obtain best possible delivery system is within the skill of the art and applicant has not shown any unexpected results using the broad claimed percentages.

7. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 636 363 or JP 09-263579 cited above, further in view of Gold (6,465,188).

The teachings of EP and JP have been discussed above. Although these references teach the negatively charged neuraminic acid, they do not teach the inclusion of negatively charged fatty acids.

Gold while disclosing nucleic acid ligand complexes teaches that the efficiency of delivery of the complex may be optimized by using components which enhance the fusion of the membranes and free fatty acids (carboxylate moieties) are fusion enhancing agents (note col. 14, line 66 through col. 15, line 20).

The inclusion of fatty acids in the compositions of EP or JP would have been obvious to one of ordinary skill in the art since free fatty acids enhance the delivery of nucleic acid by promoting fusion as taught by Gold.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments with regard to EP and JP have been addressed above. Applicant provides no specific arguments with regard to Gold. The rejection is maintained.

10. Claims 6 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 636 363 in combination with either Schneider (6,258,378) and Malone (PNAS, vol. 86, pp.6077-6081, 1989).

The teachings of EP have been discussed above. Although EP teaches the use of either a primary, secondary, tertiary or quaternary amine, it does not teach claimed quaternary ammonium compounds in claim 6.

Schneider while disclosing liposomal compositions for the delivery of biologically active substances to target sites in the body of patients teaches that cationic lipids such as dimethylammoniumpropane (TAP) and dioleoyloxy propyl trimethylammonium chlorides (DOTMA) are useful in the formation of liposomes (note abstract, col. 6, lines 56-59).

Malone teaches that cationic lipids such as DOTMA enhance the liposome-mediated transfection of nucleic acids (note the abstract and the discussion).

The use of specific cationic ammonium lipids in the liposomes of EP would have been obvious to one of ordinary skill in the art since Schneider teaches their common use in the liposomes to deliver active agents to the target sites and Malone teaches that if the drug involved is a nucleic acid, the cationic lipids enhance the transfection ability of the liposomes.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments with regard to EP and JP have been addressed above. Applicant provides no specific arguments with regard to Schneider and Malone. The rejection is maintained.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK